REMARKS

Claims 1-48 were pending prior to entry of the instant amendment. Claims 5-8 and 27-46 have been withdrawn as being directed to a non-elected invention.

By virtue of this amendment, claims 1, 2, 3, 4, 9-21, 24, 26 and 47-48 have been amended; and claims 22, 23 and 25 have been cancelled, without prejudice. Claims 1, 2, 3, 4, 9-21, 24, 26 and 47-48 have been amended to recite a composition comprising an isolated immunostimulatory sequence (ISS), and a pharmaceutically acceptable excipient wherein the ISS is less than about 200 nucleotides in length. Support for compositions and pharmaceutically acceptable excipients can be found at least at page 21, lines 10-18, and 74, lines 1-5. Support for less than about 200 nucleotides in length can be found at least at page 37, lines 24-28. Regarding claim 26, support for an ISS linked to a MC can be found at least at page 61, lines 6-19. Applicants reserve the right to prosecute the subject matter of amended or cancelled claims in related applications.

Applicants have amended the specification at pages 45-46 to eliminate a hyperlink as requested by the Examiner. Pursuant to the Examiner's request, Applicants will correct any errors in the specification of which they become aware during the prosecution of the instant application.

Claim Objections

The Examiner has objected to claims 9-25 and 47-48 as allegedly being drawn to non-elected subject matter. Claims 9, 11-12, 14-20, and 47 have been amended to remove dependency upon non-elected claims. Claim 24 is dependent upon claim 1. Therefore, this objection has been obviated. Applicants reserve the right to prosecute non-elected subject matter in related applications. Applicants will address cancellation of additional non-elected subject matter at such time as otherwise allowable subject matter is determined.

Section 101 Rejection of Claims

Claims 1-4, 9-19, 22-26 and 47 are rejected as drawn to non-statutory subject matter. Applicants traverse this rejection. Solely in an effort to expedite prosecution, Applicants have amended claims to recite a composition and an isolated immunostimulatory sequence, thereby obviating this rejection of claims. Applicants request withdrawal of this Section 101 rejection of claims.

Section 112, First Paragraph Rejection of Claims

I. Claims 1-4, 9-26, 47-48 are rejected under Section 112, first paragraph, written description. The Examiner alleges that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors at the time the application was filed had possession of the claimed invention. Applicants traverse this rejection of claims. The Examiner has the initial burden of presenting evidence or reasons why a person skilled in the art would not recognize that the written description of the invention provides support for the pending claims. The relevant question is whether there is sufficient written description to inform a skilled artisan that Applicants were in possession of the claimed invention as a whole at the time the application was filed. The Examiner has not met the burden of presenting evidence or reasons why a person skilled in the art would not recognize that the written description of the invention provides support for the pending claims. One of skill in the art would recognize that Applicants were in possession of the claimed invention.

The Examiner alleges at page 5 of the instant Office Action that the claims are drawn to "immunomodulatory polynucleotides". The Examiner points to the specification at page 12, lines 11-25 as teaching that immunomodulatory polynucleotides include immunostimulatory as well as immunosuppressive effects. Applicants invite the Examiner's attention to the claimed invention which recites, in part, a composition comprising an isolated immunostimulatory sequence (ISS) comprising the formula recited. Immunomodulatory polynucleotides are described throughout the specification, in particular at page 22 through page 38. ISS are described throughout the specification, including at page 23, line 1, through page 36. Compositions comprising ISS are

described throughout the specification including, for example, at page 21, line 5 through page 22, line 19. The Examiner alleges that the specification is devoid of description of any polynucleotides that perform down regulation of the immune response by known mechanisms of the art. The fact that a mechanism of action for an immune response may be known or not known is not the test for compliance with the written description requirements of Section 112, first paragraph. Applicants submit that there is sufficient written description to inform a skilled artisan that Applicants were in possession of the claimed invention as a whole at the time the application was filed.

Therefore, the Examiner has not met the burden of presenting evidence or reasons why a person skilled in the art would not recognize that the written description of the invention provides support for the pending claims. The claims are in compliance with Section 112, first paragraph written description requirements.

II. Claims 1-4, 9-26 and 47-48 are rejected under Section 112, first paragraph, enablement. The Examiner alleges at page 5 that the specification while being enabling for an isolated ISS consisting of SEQ ID NOs:18, 38 and 59, wherein the ISS is fully modified phosphorothioate oligonucleotide and increases IFN-gamma or IFN-alpha, and compositions comprising such and is optionally complexed with a cationic poly microsphere, is not enabled for immunomodulatory nucleic acids, immunostimulatory nucleic acid in general, and biodegradable microcarriers in general, or oligoriboxynucleotides, ISS linked to cationic by any means.

Applicants traverse this rejection of claims. To comply with the requirements of Section 112, first paragraph, a specification must adequately teach how to make and how to use the claimed invention, throughout its scope without undue experimentation. Those of skill in the art at the time of the filing would understand how to make and use the claimed invention without undue experimentation.

The Examiner states at page 6 of the Office Action that the claims are drawn to immunomodulatory polynucleotides. Applicants point out that claim 1 recites, in part, a composition comprising an isolated immunostimulatory sequence (ISS), and a pharmaceutically

acceptable excipient, wherein the ISS is less than about 200 nucleotides in length and comprises the recited formula.

The Examiner alleges at page 6 of the Office Action that the teachings of the specification are limited to a demonstration that fully modified phosphorothioate oligodeoxynucleotides of SEQ ID NOs: 18, 38 and 59 provide for immunostimulation by means of increased antigen-specific IgG when administered in conjunction with antigen. Applicants do not agree that the teachings of the specification are limited to fully modified phosphorothioate oligodeoxynucleotides of SEQ ID NOs: 18, 38 and 59 that provide for immunostimulation by means of increased antigen-specific IgG when administered in conjunction with antigen. ISS and/or immunomodulatory polynucleotides may or may not be phosphate modified (see the specification at page 34, lines 1-5);[1] the specification teaches how to make and use various ISS polynucleotides (see the specification at pages 22-36 and page 66-73); and the compositions may be administered with or without antigen (see the specification at page 38, lines 16-19).[2]

The Examiner also alleges at page 6 of the Office Action that the response of SEQ ID NOS other than 18, 38 and 59 in producing increased levels of INF is not indicative of an immune response. The Examiner has neither provided evidence of this alleged theory that increased levels of INF are not indicative of an immune response, nor provided identification of the sequences being referenced. The Examiner alleges that the source of IFN-gamma and IFN-alpha produced is not taught by the specification. To comply with the requirements of Section 112, first paragraph, a specification must adequately teach how to make and how to use a claimed invention, throughout its scope without undue experimentation. The fact that the source of IFN-gamma and IFN-alpha produced is or is not taught by the specification in itself does not support a finding of non-enablement of the pending claims.

[1] The specification at page 34, lines 1-5 states that the ISS and/or immunomodulatory polynucleotide can also contain phosphate-modified oligonucleotides (emphasis added).
[2] The specification at page 38, lines 16-19 states that an antigen may be co-administered with an immunomodulatory polynucleotide (emphasis added).

The Examiner states at page 7 of the Office Action that the data presented in the specification does not demonstrate that a Th1 response was generated. The claimed invention does not recite generation of a Th1 response.

The Examiner at page 7 of the Office Action alleges that the specification does not contain an assay that indicates that the claimed nucleic acids possess the ability to down regulate any immune response. Such assays that measure the ability of a substance to down regulate an immune response are known in the art. The claimed invention recites, in part, a composition comprising an isolated immunostimulatory sequence (ISS), and a pharmaceutically acceptable excipient, wherein the ISS is less than about 200 nucleotides in length and comprises the recited formula. Assays for measuring the ability of an ISS to stimulate the immune response are described herein and are known in the art.

The Examiner alleges at page 8 of the Office Action that the specification as filed is devoid of data that indicates that the claimed ISS nucleic acids possess immunomodulatory activity or immunostimulatory activity as claimed. Applicants disagree with this statement and invite the Examiner's attention to the Examples which describe *in vitro* and *in vivo* immunomodulation in response to administration of ISS-containing polynucleotides. With respect to coupling to microspheres, the Examiner alleges at page 9 of the Office Action that in the absence of demonstrated activity of a number of different ISS complexes, the claims are not enabled. To comply with the requirements of Section 112, first paragraph, a specification must adequately teach how to make and how to use the claimed invention, throughout its scope without undue experimentation. Applicants respectfully submit that the test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The Examiner alleges at page 8 of the Office Action that there is no evidence of record that any sequence that is not fully phosphorothiolated provides for immune stimulation in any model, yet does not provide any objective evidence of this alleged theory. The specification teaches that an ISS may or may not be modified. See the specification at page 34, lines 1-5. For a *prima facie* case on non-enablement, the burden is on the Office to demonstrate that there is a reasonable basis to question the presumptively sufficient disclosure made by applicant. See, for example, In re Wright, 27 USPQ2d 1510 (Fed. Cir. 1993). The Examiner has not met this burden. The Examiner states at page 9 of the Office Action that the length of the oligonucleotide impacts its ability to induce interferon production in mixed splenocyte cultures. Applicants point out that the claimed invention does not recite interferon production.

Applicants respectfully submit that the Examiner has not produced adequate evidence to support a lack of enablement and therefore, a *prima facie* case of non-enablement has not been established. The specification teaches how to make and use the claimed invention without undue experimentation. Thus, Applicants respectfully submit that the pending claims are in compliance with the enablement requirements.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph, written description and enablement.

Section 102 rejection of claims

I. Section 102(b) rejection of claims 1-3, 7, 9, 11, 15-19 and 22 as allegedly anticipated by Jefferson et al. US Patent No. 5,879, 906, issued March 9, 1999.

Applicant traverses this rejection of claims. For a claim to be anticipated by a reference, the reference much teach each and every element of the claim.

Claim 1 recites, in part, a composition comprising an isolated immunostimulatory sequence (ISS), and a pharmaceutically acceptable excipient wherein the ISS is less than about 200

nucleotides and comprises the recited formula. Each and every element of the claimed invention is not present in the cited reference and therefore cannot anticipate the claimed invention.

II. Section 102(e) rejection of claims 1-3, 15-19, 22, 23, 26, 48 and 49 as allegedly anticipated by Doucette-Stamm et al. US Patent No. 6,800,744.

Applicant traverses this rejection of claims. For a claim to be anticipated by a reference, the reference much teach each and every element of the claim.

Claim 1 recites, in part, a composition comprising an isolated immunostimulatory sequence (ISS), and a pharmaceutically acceptable excipient wherein the ISS is less than about 200 nucleotides and comprises the recited formula. Each and every element of the claimed invention is not present in the cited reference and therefore cannot anticipate the claimed invention.

Applicants request withdrawal of the Section 102 rejections of claims.

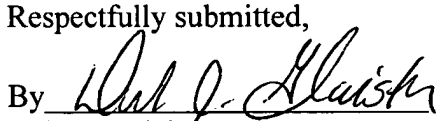
CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 377882001800. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: January 4, 2006

Respectfully submitted,

By 

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